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Prevalence of Epilepsy in Podgorica, Montenegro

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A B S T R A C T

The purpose of this study was to assess for the first time the prevalence of epilepsy in the capital of Montenegro and to describe the clinical and epidemiological profile of the disorder. A door-to-door screening was performed on population of 6 randomly selected areas of Podgorica (capital of Montenegro) using validated screening questionnaire. In phase 1, the screening by questionnaire of 4007 individuals identified 307 suspected cases of epilepsy. Four of them dropped out of further investigation just before entering the phase 2. In phase 2, the remaining 303 suspected cases were first examined by general practitioner and then by an epileptologist, on two follow-up visits. The confirmation of epilepsy was based on clinical examination. Electroencephalogram (EEG), computed tomography (CT) and/or magnetic resonance imaging (MRI) were also used, resulting in 29 persons being diagnosed with epilepsy. An overall prevalence of 7.2 cases per 1000 inhabitants was calculated (CI 95% 5.0–10.0). Majority of them had been previously diagnosed (86.20%), 27 had active epilepsy and over a half of them had multiple antiepileptic drugs (65.51%). Referring to the 27 patients with active epilepsy, the predominant seizure type was focal (all types) in 14 (48.27%), generalised idiopathic seizures in 11(37,93%) and undetermined in 2 (6.89%). Cause of epilepsy was known in 10 patients. EEG abnormalities were found in almost all patients (89.65%). CT anomaly was determined in 9 whereas only 1 patient had an abnormal MRI finding. The estimated prevalence of epilepsy indicated higher rates compared to neighboring counties and the rest of the Europe, but limitations of the study (high rejection rate and stigma) should be taken into consideration.

Key words: *epilepsy, active epilepsy, door-to-door screening, prevalence, Montenegro*

Introduction

Epilepsy is a worldwide, chronic, multifactorial neurological disorder affecting over 50 million people[1].

The mean prevalence rate for active epilepsy in developed countries varies between 4 and 10 per 1000 [2]. In a systematic review by Forsgren[3] it was found that the range for prevalence rates in Europe was 3.3−7.8 per 1000 with a median prevalence rate of active epilepsy 5.2 per 1000. Higher prevalence rates have been reported from resource poor countries, ranging from 10 to 40‰[4]. Regardless of apparent disparities among rich and resource poor countries, these numbers clearly show the enormous socioeconomic burden epilepsy carries with itself.

The data from some eastern Mediterranean countries are missing including Montenegro. Epidemiological data on epilepsy are deficient and currently national registry as well as control program are lacking. Population based prevalence study from neighboring Croatia suggests prevalence rates between 4.8 and 5.5/1000, which is in accordance to the findings from other European countries[5]. Montenegro is in many aspects very similar to Croatia suggesting that similar prevalence rates are to be expected.

The aim of this study was to obtain for the prevalence rate of epilepsy in the capital of Montenegro and to describe the clinical and epidemiological profile of the disorder.

Methods

We conducted a door-to-door survey in six areas: four urban and two rural areas of Podgorica in order to investigate the prevalence of epilepsy. These areas were generally chosen because they included different socioeconomic classes and local health centers were easily assessable. The population of Podgorica, the capital of Montenegro, is about 185.000 people which is 30% of total Montenegrin population[6].

Our sample included only participants aged 18 to 80 years of age, which constitute around 130.000 people.

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Written informed consent was obtained from all subjects who were willing to participate to enrolment. A person who answered positively to at least one of the 13 questions of the screening questionnaire (Table 1) was considered as a suspected epilepsy case.

TABLE 1
SCREENING QUESTIONNAIRE FOR EPIDEMIOLOGY OF EPILEPSY

Unique patient ID: / / / / / /

Name:_____ Sex:_____ Age:____

Occupation:_____ Address:_____

Questionnaire:

1. Have you ever had attacks of shaking of the arms or legs which you could not control?
2. Have you ever had attacks in which you fall and become pale?
3. Have you ever lost consciousness?
4. Have you ever had attacks in which you fall with lost consciousness?
5. Have you ever had attacks in which you fall and bite your tongue?
6. Have you ever had attacks in which you fall and lose control of your bladder?
7. Have you ever had brief attacks of shaking or trembling in one arm or leg or in face?
8. Have you ever had attacks in which you lose contact with the surroundings and experience abnormal smells?
9. Have you ever been told that you have or had epilepsy or epileptic fits?
10. Have you ever had attacks in which you lose contact with your surroundings and experience a sensation in which objects change shape or size?
11. Did you ever have attacks of convulsions in fever before the age of 5?
12. Have you ever suddenly in a daze or amazement, lost something from your hand during an activity, writing or eating?
13. Have you ever had suddenly in a daze, smack, purposeless activity of hands which you subsequently have no memory?

For those with definite or possible epilepsy:

1. Onset age:_____
2. Number of attacks:
   Recent 1 year: ←=have attacks (____times); ↑=no attack
   Recent 2 years: ←=have attacks (____times); ↑=no attack
   Recent 5 years: ←=have attacks (____times); ↑=no attack
3. Are there any causes of attack? _____
4. Did the patient take any treatment?
   (1) Never accepted any treatment: 1 = Yes; 2 = No
   (2) To be Treated: 1 = Yes; 2 = No
   If answer yes: 1 = Western medicine; 2 = Traditional medicine
   Drug name and dosage: _____
   Effect: 1 = Excellent; 2 = Good; 3 = No effect
   Treatment assessment: 1 = Regular; 2 = Irregular
   (3) Last week: 1 = treatment; 2 = Not treatment
   Effect: 1 = Excellent; 2 = Good; 3 = No effect

Investigator:_____ Date:_____

Check result:

Conclusion:

1 = Diagnose epilepsy 2 = Excluded epilepsy

Seizure type:

1. Simple Partial Seizures 2. Complex Partial Seizures 3. Secondarily Generalized Seizures
4. Generalized Tonic-clonic seizures 5. Absences 6. Others (Myoclonic, Atonic etc)

Checked by Dr._____ **Date:**_____

Clinical and epidemiological definitions

Following definitions were used to classify epilepsy as well as types of medication in all cases:

1. Epilepsy was defined as a condition characterized by recurrent epileptic seizures, unprovoked by any immediate identified cause. Multiple seizures occurring in a 24-hour period were considered as a single event. An episode of status epilepticus was considered as a single event. Individuals who had had only febrile seizures, seizures during pregnancy, or seizures due to alcohol or substance abuse or acute psychiatric illness were excluded from this category.
2. Active epilepsy: any patient who has had recurrent unprovoked seizures with an interval between them of 24 hours or more in the previous 12 months.
3. Inactive epilepsy: any patient who has had recurrent unprovoked seizures with an interval between them of 24 h or more, but who has been seizure-free for the previous 36 months.
4. Adequate epilepsy treatment: any patient with active epilepsy regularly using appropriate antiepileptic drugs (AEDs) as mono-or polytherapy at standard dosage is defined as having adequate epilepsy treatment [7]
5. Monotherapy: any patient who is taking just one AED is defined as taking monotherapy.
6. Polytherapy: any patient who is taking more than one AED is defined as taking polytherapy.

Design of a study

A two phase approach was used to identify patients with epilepsy (Figure 1):

Phase 1 – through a door-to-door survey a screening questionnaire was used to identify potential patients with epilepsy. This phase was carried out between June and December 2013. For this survey, we used a validated epidemiological questionnaire (with sensitivity 95.8% and specificity 97.8%) for the identification of cases of epilepsy [8]. During a door- to-door survey all inhabitants of selected six areas were interviewed by a trained medical doctor. They made sure that participants understood all the questions, they provided additional explanations but were not allowed to influence the answers of participants in any way. Name, age, gender, address and telephone number were taken from all interviewed participants for the purpose of further investigation. Each sheet had its code and those codes were given to the participants.

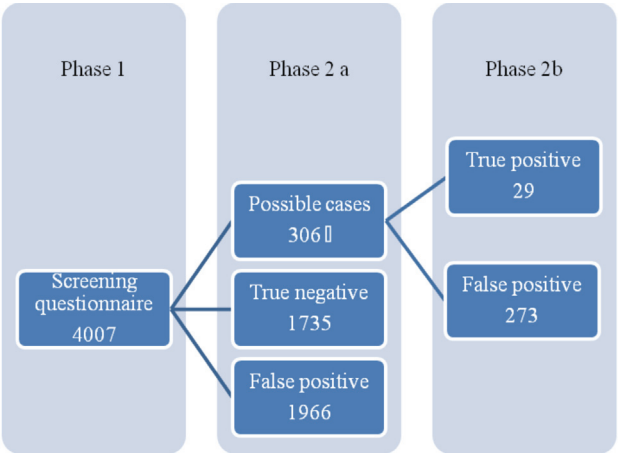

Fig. 1. Screening survey about epilepsy conducted in Podgorica, Montenegro.

If no response was obtained on the first visit to a flat or a house, two further visits were made and if still there were no response the unit was considered as nonresponsive. Also if participants did not want to participate, even after detailed oral explanation, were also considered nonresponsive.

Phase 2 – in the first step of phase 2 those who screened positive in phase 1 were sent to the nearest general practitioner, who performed routine physical examination as well as biochemistry analysis in order to rule out other diagnosis which can mimic epilepsy. Those who were still considered as possible patients with epilepsy were then sent to a neurologist, trained in epilepsy, to confirm or refuse the diagnosis based on clinical examination and detailed interview (second step of phase 2).

An EEG (standard and prolonged recording; Nicolet One® EEG) was performed in all patients, as well as CT (Siemens). MRI (Siemens, 1.5 Tesla) was done in all patients with negative CT. Clinical examination and imaging were completed on initial visit and on second follow up final diagnosis was made. People not diagnosed as having epilepsy were considered false positive.

Statistics

Data were coded and entered into the computer using Excel Programme and were analyzed by "Statistical Package for Social Sciences" (SPSS) 16.0 statistical software. (SPSS Inc., Chicago, IL). Prevalence was estimated on the basis of the number of true positive cases divided by total number of people studied expressed as n/1.000 (with a 95% confidence interval estimated using Wilson's method). The results are presented using means and frequencies.

Results

In a phase 1 a total of 4007 people were interviewed. Rejection rate was very high (43% of all subject were willing to participate), especially among suburb. The mean age of participants was 39.18+/–19.33 (SD) with majority of participants being female (63.1%). 2272 (56.7%) interviewees screened positive.

In a first step of phase 2, all participants who screened patients were seen by a general practitioner who referred 306 (7.6%) to an epileptologist as a potential cases of epilepsy. Four patients dropped out from further inves-

tigation. A neurologist evaluated the diagnosis in remaining 303 subjects, identifying 29 patients as true positive. Thus, from a study population of 4007, 29 patients with epilepsy were identified yielding an overall prevalence of 7.23% (95% CI 5.0–10.0). Majority of patients (86.2%) had already been diagnosed with epilepsy and the remaining 4 had inactive epilepsy. Twenty two patients (75.8%) were diagnosed after first confirmation visit and 7 patients after the second.

Nineteen of 29 patients were female (65.5%). The mean age of patients was 43.1+/–18.1 (SD). The most frequent age range among patients with epilepsy was 18–34, as well as over 65. Socio-demographic characteristics of patients with epilepsy are given in Table 2.

In regard to etiologic classification, the cause of epilepsy was found in just over a third of patients (34.4%). 13 patients (44.8%) had idiopathic generalized syndrome while 6 patients (20.6%) had cryptogenic epilepsy. The causes of symptomatic epilepsy in our sample were the following: stroke (30%), primary brain tumor and traumatic brain injury (20% respectively), metastases, encephalitis and congenital anomalies (10% respectively). Five patients with idiopathic generalised syndrome had a family history of epilepsy.

TABLE 2
SOCIO-DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH EPILEPSY

Gender	n/%
Male	10 (34.48%)
Female	19 (65.52%)
Residence	
Urban	17 (58.62%)
Rural	12 (41.37%)
Age	
18–24	6 (20.69%)
25–34	6 (20.69%)
35–44	4 (13.79%)
45–54	2 (6.90%)
55–64	4 (13.79%)
>65	7 (24.14%)
Level of education	
Elementary school	6 (20.69%)
Secondary school	14 (48.28%)
Faculty	9 (31.03%)
Employment	
Employed	8 (27.58%)
Unemployed	14 (48.28%)
Retired	7 (24.14%)
Marital status	
Married (female)	5 (17.24%)
Married (male)	5 (17.24%)
Single (female)	13 (44.83%)
Single (male)	4 (13.79%)
Divorced	1 (3.45%)
Widower	1 (3.45%)

Focal epilepsy (all types, 14 patients, 48.2%) was more common than generalised epilepsy (13 patients, 44.85%). The remaining 2 cases (6.8%) could not be classified as either generalized or partial using ILAE classification [9]. Among patients with partial seizures the most common type was complex partial seizures (9 patients, 64.2%). They were more likely to be found among older. In one patient with a generalised tonic-clonic seizure, the use prolonged EEG recording that the seizure had a focal onset.

Epileptiform EEG changes were found in 26 epilepsy patients. CT revealed abnormalities in 9 patients (31%). In 3 cases CT with application of contrast was performed in order to reveal the etiology of seizures. MRI was performed in 14 patients but only one patient had MRI abnormality found.

Twenty seven patients (93.10%) had active epilepsy. The mean duration of epilepsy was 6.24+/– 4.13 years (SD). Over 60% of patients were on multiple antiepileptic drugs. The most frequently used antiepileptic drugs (AED) were phenobarbital, carbamazepine, sodium valproate, lamotrigin, topiramate and levetiracetam. The most common combination of AEDs were sodium valproate and topiramate, topiramate and lamotrigine, carbamazepine and topiramate, carbamazepine and levetiracetam, sodium valproate and levetiracetam.

Discussion and Conclusion

This study was designed to provide the first prevalence rate on epilepsy in Podgorica, Montenegro.

Our door-to-door survey revealed a prevalence of epilepsy among the interviewed population of 7.2 cases per thousand. Compared to some [5–10] but not all parts of neighboring Croatia [15] and other more developed European countries,[11–14] our results showed a pattern towards higher prevalence. We feel that this result is rather due to low sample size owing to low willingness to participate and compliance of interviewees, especially in rural areas. Just over 43% of all inhabitants were willing to take the survey. Majority of those who were finally confirmed as epilepsy cases had already been diagnosed. We believe that stigma and prejudice were the possible explanations for the low response rate.

Distribution of our patients with epilepsy was binominal, with the majority of patients being in their third or fourth decade of life and older than 65. This result is in accordance with the finding of Hauser[18], although Montenegro is more of a developing country which by literature shows a different distribution pattern.

The cause of epilepsy was found in over a third of patients (34.4%). Well defined risk factors like stroke and traumatic brain injuries were found in half of these patients, predominantly male. Our result thus supports

findings from other bigger surveys which concluded that stroke[12,19–20] and especially TBI contribute to the occurrence of seizures and epilepsy.

The predominant seizure types among our patients were partial seizures, predominantly among older. The pattern observed in the distribution of localization-related, generalized and undetermined epilepsies among cases in this sample is consistent French[21], Swedish[12] and Finnish[13].

Over 90% of diagnosed patients had active epilepsy and they were all under treatment. Unlike many resource poor and developing countries[22] antiepileptic drugs are not limited in Montenegro. Any patient with a diagnosis of epilepsy will be provided with AED, free of charge, even with new AEDs like levetiracetam and pregabalin. This result would therefore suggest that treatment gap does not exist in Montenegro. However, authors disagree. Treatment gap is a global problem and regardless of reason even a small percentage of people with epilepsy, at least initially, would be left untreated.

This was a first study to estimate the prevalence of epilepsy is Montenegro. It was performed using a door-to-door screening procedure, an approach promoted by International League Against Epilepsy.[17] However, the power of the study is limited by the low response rate of interviewees. The study showed a pattern towards higher prevalence of epilepsy, although in many other aspects the results were in according to those reported from similar studies. Study also brought to light the inevitable problem of stigmatization, probably resulting in low participation rate. Capture-recapture technique should be implemented in future in order to yield more precise prevalent rate. Also, information campaigns should be enforced in order to fight stigma and build basis for better community health.

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RASPROSTRANJENOST EPILEPSIJE U PODGORICI (CRNA GORA)

SAŽETAK

Svrha ovog istraživanja bila je po prvi puta procijeniti učestalost epilepsije u glavnom gradu Crne Gore i opisati klinički i epidemiološki profil poremećaja. Istraživanje od vrata do vrata je provedeno na populaciji od 6 slučajno odabranih područja Podgorice (glavni grad Crne Gore), uz upotrebu potvrđenih upitnika. U fazi 1, selektiranjem pomoću upitnika od 4007 osoba identificirano je 307 osoba na koje se sumnjalo da pate od epilepsije. Četvero od njih je odustalo iz daljnje istrage neposredno prije ulaska u fazu 2. U fazi 2, preostalih 303-oje sumnjivih slučajeva su prvo pregledane od strane liječnika opće prakse, a zatim od strane epileptologa u još dva navrata. Potvrda epilepsije temeljila se na

kliničkom pregledu. Elektroencefalogram (EEG), kompjutorizirana tomografija (CT) i / ili magnetska rezonancija (MRI) su također korišteni, što je rezultiralo s dijagnozom epilepsije kod 29 osoba. Ukupna učestalost od 7,2 slučajeva na 1000 stanovnika je izračunata (CI 95% 5.0–10.0). Većina od njih je već prethodno bila dijagnosticirana (86,20%), 27 je imalo aktivnu epilepsiju i više od polovice ispitanih su korstili više vrsta antiepileptika (65,51%). Pozivajući se na 27 bolesnika s aktivnom epilepsijom, tip napadaja koji je prevladavao je bio žarišni (sve vrste) kod 14 ispitanika (48,27%), generalizirani napadaji idiopatska kod 11 ispitanika (37,93%), te neutvrđeni kod 2 ispitanika (6,89%). Uzrok epilepsije je poznat kod 10 bolesnika. EEG abnormalnosti nađene su kod gotovo svih bolesnika (89,65%), a CT anomalija utvrđena je kod 9, dok je samo jedan bolesnik imao abnormalan MRI nalaz. Procijenjena prevalencija epilepsije pokazala veće stope u usporedbi sa susjednim županijama i ostatka Europe, ali ograničenja istraživanja (visoka odbacivanje stopa i stigma) treba uzeti u obzir.